Office of Prevention, Pesticides, and Toxic Substances

MEMORANDUM

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SUBJECT: Review of Urea, as an Active and Inert Ingredient

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This memorandum addresses (1) the TRED (Report on FQPA Tolerance Reassessment Progress and Interim Risk Management Decisions) for the inert ingredient urea in formulation (CAS 57-13-6).

Introduction

Urea is an inert that is added to pesticide formulations. EFED was not provided with name(s) of active ingredients that are formulated with urea nor the amounts that may be found in formulations. Urea solution reduces the ice-nucleating activity of ice-nucleating bacteria which are naturally present on leaf surfaces.

Tier I estimated environmental concentrations for urea used on terrestrial crops and estimated maximum applications to avoid exceeding terrestrial and aquatic toxicity levels. The FQPA Index Reservoir Screening Tool (FIRST)[1] was used to estimate drinking water concentrations and the GENERIC Estimated Environmental Concentration (GENEEC 2.0)[2] model was used to estimate the surface water concentrations for urea to establish risk to aquatic organisms. The SCI-GROW[3] model was used to estimate groundwater drinking water concentrations. ELL-FATE model is used to estimate risk to bird and mammals.

The Food and Drug Administration (FDA) has affirmed that this chemical is generally recognized as safe (GRAS) as a direct human food ingredient.

Conclusions

The Use of urea as an inert ingredient is not expected to cause acute risk to freshwater fish and invertebrates, and birds when applied at 12.5 lb/A. Toxicity data are not available to assess chronic risk to freshwater organisms, acute and chronic risks to estuarine/marine organisms, and chronic risks to terrestrial organisms.

Table 1. Estimated environmental concentrations (ppb) of urea in surface and groundwater.

Scenario	peak	long term average	use(s) modeled	PCA
Surface water (FIRST)	53.9	0.107	1 application @ 1 lb/acre	0.87
Surface water (GENEEC)	33.2	0.37	1 application @ 1 lb/acre	
Groundwater	0.002		1 application @ 1 lb/acre	

Environmental Fate

EFED has no fate data for Urea. Information on the environmental fate was found in previous EFED reviews and the open literature (http://www.toxnet.nlm.nih.gov October 2001).

Available data from literature reviews shows that urea degrades rapidly in most soils[4-6]. In general, urea is rapidly hydrolyzed to ammonium through soil urease activity. In various soils, complete hydrolysis may occur completely within 24 hrs[4], however, the rate of hydrolysis can be much slower depending upon soil type, moisture content, and urea formulation. For example, increasing the pellet size of urea fertilitizers can decrease the urea decomposition rate from days to weeks. Soil adsorption studies have demonstrated that urea adsorbs very weakly to soil[7]; therefore, leaching is possible. Ultimate urea degradation produces ammonia and CO_2 as volatile products[8].

Biodegradation is expected to be the major fate process in the aquatic environment. Various screening studies have demonstrated that urea can biodegrade readily[9-13] with the release of CO_2 and ammonia. The rate of biodegradation generally decreases with decreasing temperatures[12]; under cold winter-like conditions, biodegradation may be relatively slow (0-6% per day)[12]. The presence of naturally-occurring phytoplankton increases the degradation rate[10,13] because phytoplankton use urea as a nitrogen source[10] and because urea is decomposed by phytoplankton photosynthesis[13]. In phytoplankton-rich waters, degradation occurs much faster in sunlight than in the dark[13].

Abiotic hydrolysis of urea occurs very slowly in relation to biotic hydrolysis[14]. Abiotic hydrolysis yields ammonium carbamate which decomposes to form CO_2 and ammonia[14]; the enzyme urease catalyzes urea hydrolysis.

In one photodegradation study using a silica gel adsorbent[9] only 0.2% of applied urea photomineralized after a 17-hr irradiation with a UV lamp (>290 nm).

The adsorption of urea was measured in six different British soils with organic carbon contents ranging from 1.76 to 36.5%. No adsorption was measurable in five of the soils[15], in the sixth soil (36.5% organic carbon), a K_{OC} of 8 can be determined from the measured Freundlich isotherm[16].

Water Resources

-Surface Water

Monitoring

At the present time, the EFED has no monitoring data on the concentrations of urea in surface water.

Modeling

Surface water concentration estimates were modeled for the use of urea as an inert using FIRST and GENEEC Tier I models. The input parameters used in simulations are shown in Tables 2 and 3.

Table 2. Urea input parameters for FIRST.

Parameter	calculations/value	source
Crop name	N/A	
application rate (lb/acre)	1	
interval between applic. (day)	N/A	
Max No. application	1	
PCA factor (decimal)	0.87 (default)	Effland et al[17] (2000).
Koc (mL/g)	8	Hance (1965).
soil aerobic met. $t_{1/2}$ (d)	1 X 3	Scheunert I. (1987); FIRST User Manual.
pesticide to be wetted-in ?	No	EPA Reg. Lable No. 688915
method of application	aerial	EPA Reg. Lable No. 688915.
solubility (mg/L)	5.45×10^5	Yalkowsky S.H. (1989)[18].
aerobic aquatic met. $t_{1/2}$ (d)	0.042 (assumed to be 1 hour: readily degraded)	Freitag D. (1985).
hydrolysis (pH 7) $t_{1/2}$ (d)	1	Sankhayan et al. (1976).
aqueous photolysis $t_{1/2}$ (d)	stable (0.2% < degraded after 17 hours of radiation)	Freitag et al. (1985).

Table 3. Urea input parameters for GENEEC 2.0 modeling.

Parameter	calculations/value	source
Crop name	N/A	
application rate (lb/acre)	1	
interval between applic. (day)	N/A	
Max No. application	1	
Koc (mL/g)	8	Hance (1965).
soil aerobic met. $t_{1/2}$ (d)	1 X 3	Scheunert I. (1987); FIRST User Manual.
pesticide to be wetted-in ?	No	EPA Reg. Lable No. 688915
method of application	aerial	EPA Reg. Lable No. 688915.
Aerial droplet size distribution	fine to medium (default)	GENEEC Users Manual.
solubility (mg/L)	5.45×10^5	Yalkowsky (1989).
aerobic aquatic met. $t_{1/2}$ (d)	0.042 (assumed to be 1 hour: readily degraded)	Freitag (1985).
hydrolysis (pH 7) $t_{1/2}$ (d)	1	Sankhayan and Shukla (1976).
aqueous photolysis $t_{1/2}$ (d)	stable (0.2% < degraded after 17 hours of radiation)	Freitag (1985).

Groundwater

Monitoring

EFED has no monitoring data on the concentrations of urea in groundwater.

Modeling

The SCI-GROW model was used to estimate potential groundwater concentrations. SCI-GROW is a screening model based on a regression approach which relates the concentrations found in ground water in Prospective Ground Water studies to aerobic soil metabolism rate and soil-water partitioning properties of the chemical.

The input and output files used in SCI-GROW are shown in Appendix I.

Surface Water Ecological Exposure

To determine ecological risks from urea as an inert ingredient, estimated environmental concentrations (EECs) were generated based on an application of 1 lb/A. Results are reported in Table 4.

Table 4. Tier I upper tenth percentile EECs in Surface Water (GENEEC 2.0)

Method of Application	Application Rate (lbs/A)	Maximum (ppb)
Aerial	1	33.2

Ecological Toxicity

The following is a summary of the available ecological toxicity data submitted to the agency:

Urea: Avian Acute Oral Toxicity study with the Upland game bird (Bobwhite Quail). 1986; J. Grimes, MRID #40710801.

LD_{50}: >2250 mg/kg, CORE; Urea is practically non-toxic to Bobwhite Quail.

Urea: A Dietary LC50 Study with the Mallard Duck and Bobwhite Quail: 1986; J. Grimes, MRID #40410701, and MRID #40710901.

LC_{50} >5620 mg/kg; CORE. Urea is practically non-toxic to Mallard Duck and Bobwhite Quail.

Urea: A 96-Hour Flow-Through Acute Toxicity Test with the Bluegill Sunfish; 1986; J. Bowman, MRID# 4071401.

Urea: A 96-Hour Flow-Through Acute Toxicity Test with the Rainbow Trout; 1986; J. Bowman, MRID# 40710601.

LC_{50}: >1000 mg/L 95% C.I. CORE Urea is practically non-toxic to Bluegill Sunfish, and Rainbow Trout .

Urea: A 48-Hour Flow-through Acute Toxicity Test with the

Cladoceran (Daphnia magna); 1986; MRID# 40710501.

LC_{50}: >1000 mg/L (48-hour) 95% C.I. CORE Urea is to practically non-toxic daphnia.

Ecological Risks

Aquatic Organisms

The toxicity data indicate that urea is non toxic to aquatic organisms. Risk to aquatic organisms are determined based on risk quotient (RQ) calculations. Risk quotients are a function of the EEC and the toxicity endpoints. The RQ is compared to the level of concern (LOC) to determine risk. Based upon the available data and calculated risk quotients, exposure to urea at 1 lb/A does not exceed the acute LOC for risk to freshwater fish and invertebrates (Table 5). To determine the maximum application rate that can be applied and not cause an acute risk, the LOC for endangered aquatic species (0.05) was divided by the RQ for both freshwater fish and invertebrates. Based on this calculation and confirmatory GENEEC runs (see Attachment), EFED does not expect acute risk to freshwater fish and invertebrates at application rates of up to 12.5 lb ai/A.

Toxicity data are not available to assess chronic risk to freshwater organisms or acute and chronic risks to estuarine/marine organisms.

Table 5. Acute Toxicity of urea to Freshwater Aquatic Organisms (based on application rate of 1 lb/A).

Organism	Exposure Type	Most Sensitive Species	Toxicity (ppm)	EEC (ppm)[1]	Risk Quotient (EEC/Toxicity)
Freshwater Fish	Acute	Rainbow trout	LC_{50}= 1000	0.03	< 0.0001
Freshwater Invertebrates	Acute	*Daphnia magna*	EC_{50}= 1000	0.03	< 0.0001

[1] Maximum EEC generated using the GENEEC 2.0 model.

Terrestrial Organisms

The toxicity data indicate that urea is practically non-toxic to birds. For pesticides applied as a nongranular product (e.g., liquid, dust), the risk quotient (RQ) is a function of the estimated environmental concentrations (EECs) on food items following product application and the LC_{50} values. The RQ is compared to the level of concern (LOC) to determine risk. The RQ values indicate that use of urea at 1 lb/A does not exceed the acute level of concern for terrestrial organisms (Table 5). To determine the maximum application rate that can be applied and not cause an acute risk, the LOC for acute risk to terrestrial organisms (0.5) was divided by the RQ for birds. Based on this calculation and confirmatory EllFate runs (see Attachment), EFED does not expect risk to birds on an acute basis at application rates #12.5 lb/A.

Chronic risks to terrestrial organisms could not be determined because toxicity data are not available.

Table 5. Acute Toxicity of urea to Terrestrial Wildlife.

Animal Group	Exposure Type	Most Sensitive Species	Toxicity (mg/kg)	EEC (ppm)[1]	Risk Quotient
Birds	Acute	Mallard	LD_{50} = 5620	240	0.04

[1] **The highest terrestrial residue anticipated. RQs were calculated using ELLFate model.**

Terrestrial and Aquatic Plants

Data on the effects of urea on nontarget plants are not available. EFED does not expect risk to plants from use as an inert ingredient because review of the registered uses indicates low potential for exposure.

Uncertainties

The model FIRST is designed to yield concentration values which exceed those predicted by the linked EPA PRZM and EXAMS models for all but the most extreme sites, application patterns and environmental fate properties. PRZM/EXAMS predictions may exceed FIRST predictions under the following circumstances:

(1) Applications to crops in managed environments known to produce excessive runoff (e.g. crops grown over plastic mulch).

(2) Applications at sites with hydrologic group D soils which also receive excessively high rainfall (e.g. EFED sweet potato scenario in southern Louisiana).

(3) Multiple applications over a window of 30 days or longer in exceptionally high rainfall areas (e.g. far southeastern US).

In each of these cases, FIRST will exceed PRZM/ EXAMS estimated peak concentrations values, but not always the annual average concentration values. Even then PRZM/EXAMS would not be expected to exceed the FIRST values by more than a factor of 2.

(4) For applications of chemicals with half-life values of 5 days or less at exceptionally high runoff sites the PRZM/EXAMS concentrations values may exceed both the FIRST peak and annual average values by a factor of 2. Allowing these few exceedences for extreme conditions makes FIRST a more reasonable predictive tool for the rest of the country.

For urea, the above situations are not likely to apply, thus, we would expect FIRST estimates to exceed the Tier 2 estimates.

The SCI-GROW model (Screening Concentrations in Ground Water) is used for estimating concentrations of pesticides in ground water under "maximum loading" conditions. SCI-GROW provides a screening concentration, an estimate of likely ground water concentrations if the pesticide is used at the maximum allowed label rate in areas with ground water exceptionally vulnerable to contamination. In most cases, a majority of the use area will have ground water that is less vulnerable to contamination than the areas used to derive the SCI-GROW estimate.

The environmental fate and ecological effects data used in this assessment were supplemental (i.e., the studies were not conducted following EFED guidelines). Therefore, EFED can not conclude that the data were collected in a manner consistent with the Agency's guideline requirements.

Inert ingredients can enhance the toxicity of herbicide active ingredients to nontarget plants; therefore, this assessment may significantly underestimate the potential for adverse effects to nontarget plants. However, at this time, EFED is not aware of which formulated products will include urea as an inert.

Another area of uncertainty is the estimate of how great an application rate will exceed. While in most cases variability and slope may not matter, but we are assuming a positive correlation of application rate and effect (toxicity). So there may not be a direct positive correlation.

References

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3. Barrett, Michael. 1997. Proposal for Method to Determine Screening Concentration Estimates for Drinking Water Derived from Ground Water Sources. Internal EPA Memorandum to Joe Merenda dated June 30, 1997.

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6. Scheunert I. 1987. Chemosphere 16: 1031-1041.

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APPENDIX I

FIRST output file

```
RUN No.   1 FOR urea            ON                 * INPUT
VALUES *
----------------------------------------------------------------
RATE (#/AC) No.APPS & SOIL  SOLUBIL  APPL TYPE  %CROPPED INCORP
ONE(MULT)  INTERVAL   Koc   (PPM )   (%DRIFT)    AREA    (IN)
-----------------------------------------------------------------
1.000(  1.000)  1 1   8.0  *******      AERIAL(16.0)  87.0    .0


FIELD AND RESERVOIR HALFLIFE VALUES (DAYS)
----------------------------------------------------------------
METABOLIC  DAYS UNTIL  HYDROLYSIS   PHOTOLYSIS METABOLIC COMBINED
(FIELD)  RAIN/RUNOFF  (RESERVOIR)  (RES.-EFF)   (RESER.)
(RESER.)
----------------------------------------------------------------
3.00        2          N/A       .00-     .00       .04        .04


UNTREATED WATER CONC (MICROGRAMS/LITER (PPB))    Ver 1.0 AUG 1,
2001
----------------------------------------------------------------
       PEAK DAY  (ACUTE)      ANNUAL AVERAGE (CHRONIC)
        CONCENTRATION             CONCENTRATION
---------------------------------------------------------------
        53.916                      .107
```

GENEEC 2.0 input and output files

```
RUN No.   1 FOR urea      ON                 * INPUT VALUES *
-----------------------------------------------------------------
```

```
RATE (#/AC)   No.APPS &   SOIL  SOLUBIL   APPL TYPE NO-SPRAY INCORP
ONE(MULT)    INTERVAL    Koc   (PPM )     (%DRIFT)   (FT)     (IN)
------------------------------------------------------------------
1.000(  1.000)  1    1   8.0  *******   AERL_B( 13.0)     .0    .0
```

```
FIELD AND STANDARD POND HALFLIFE VALUES (DAYS)
------------------------------------------------------------------
METABOLIC   DAYS  UNTIL   HYDROLYSIS    PHOTOLYSIS    METABOLIC
COMBINED
(FIELD)   RAIN/RUNOFF   (POND)     (POND-EFF)    (POND)     (POND)
------------------------------------------------------------------
3.00        2          N/A       .00-      .00       .04        .04
```

```
GENERIC EECs (IN MICROGRAMS/LITER (PPB))      Version 2.0 Aug 1,
2001
------------------------------------------------------------------
PEAK       MAX 4 DAY     MAX 21 DAY    MAX 60 DAY    MAX 90 DAY
GEEC       AVG GEEC       AVG GEEC      AVG GEEC      AVG GEEC
------------------------------------------------------------------
33.17       8.29           1.58          .55              .37
```

SCI-GROW input and output

```
RUN No.   1 FOR urea                INPUT VALUES
------------------------------------------------------------------
APPL (#/AC)  APPL.  URATE    SOIL    SOIL  AEROBIC
RATE         NO. (#/AC/YR)   KOC   METABOLISM (DAYS)
------------------------------------------------------------------
1.000       1       1.000     8.0       1.0
```

```
   GROUND-WATER SCREENING CONCENTRATIONS IN PPB
------------------------------------------------------------------
                       .001699
-----------------------------------------------------------------
  A=       .167  B=    13.000  C=     -.778  D=     1.114  RILP=
 -.867
  F=    -2.770  G=       .002  URATE=     1.000  GWSC=
.001699
```